to twelve grains in the twenty-four hours, no toxic effects of even the slightest severity were produced, and there was no evidence of accumution in cases where the remedy was taken for from three to four months continuously.

The first effect, coming on about thirty minutes after exhibition of the dose, consists in a strengthening of the force of the heart-beats, with a slowing and regulation of the pulse in cases where this is abnormally rapid. Closely following on this, at about forty-five minutes or one hour after the dose, the arterial tension is raised, and shortly before this rise of tension, or at the same time, the surface of the skin becomes red, flushed, and moist, with, in some instances, free perspiration. During the next two or three hours, for the first part of the time, the surface of the body remains flushed and warm, the arterial tension continues to rise, or to remain at a higher level than before the dose, and the rate of the pulse to be slowed until it reaches or approaches the normal, while from the first the heart beats with increased force; the patient, meanwhile experiences a marked sense of well-being and of comfortable warmth, with, if it existed, loss of præcordial distress, irregular cardiac action, and dyspnœa. Now it seems to me that this rise of arterial pressure, with increased amount of blood sent through the skin (and kidneys), can only be explained in one way, by a special action of spartein on the medullar vasomotor centre, this centre by causing contraction of the vessels of the splanchnic area, and so diminishing the amount of blood sent through the great splanchnic vessels raises the blood-pressure, and, at the same time, an increased amount of blood is driven through the vessels of the skin and kidneys. This increased cutaneous blood-supply will be sufficient to explain the moistening of the skin that takes place, but where free sweating occurs, I think, we must also suppose a stimulation of the secreting cells of the sweat-glands by the drug.

Spartein also causes a variable increase in the amount of the urinary secretions, with increased excretion of urea, in correspondence with the increase of water, and this diuretic action we should anticipate as a consequence of the strengthened *vis a tergo*, the rise of blood-pressure, and the increased quantity of blood passing through the kidneys. This flushing of the surface was a constant result, except in a few cases. On respiration spartein produces an initial quickening, followed by a slowing, reaching or approaching to the normal rate, at the same time the respiratory movements are of greater depth.

Now some minor modifications of the above statements require notice. First, as in Gluzinski's observations, quoted above, in some cases the division of the action of spartein into three periods, an intial, and later one, of slowing of the pulse and respiration, with an intermediate period of quickening, was noticed; this effect occurred about seventy-five to ninety minutes after the dose was taken, and in only two or three patients; it was especially marked in a case of aortic regurgitation.

Secondly, the best results, in all respects, were obtained when the dose was given often; every four hours appeared the most satisfactory arrangement. Then small and large doses have a somewhat different effect, and this explains some of the discrepancies in the statements of the observers above quoted. Small doses, one-sixteenth to one-twelfth of a grain, produce the maximum effect in the regulation of the pulse. In one instance doses of one-tenth of a grain rendered a previously arhythmic pulse quite regular when large doses had failed to do so, and I had frequent occasion to note the same result. These small doses were also best for relieving palpitation, and for quieting down violent cardiac pulsation; small amounts also appeared to strengthen the force of the heart-beats, with very little raising of the arterial tension, and the stimulating cardiac action, combined with small increase of tension, will be doubtless of great service where it is important to strengthen the force of the heart-beats without increasing markedly the peripheral resistance. Larger doses, one to two grains, powerfully increase the force of the beats, but, at the same time, even more powerfully raise the arterial tension, and as an effect of this I found, in many cases, violent pulsation produced, with præcordial pain, and a strong but very tense pulse.

When the drug is taken regularly for some time, the general effect, apart from that of each individual dose, is found often to be an acceleration of the pulse and respiration-rate, giving way, after the first day or days, to a subsequent slowing.

As to accumulation, an overdose, taken for some time, appears to produce very high tension of the pulse, and, as in the case of mitral stenosis, "tightness of the chest," with sharp cutting pains and throbbing over the heart; in another case, after spartein had been taken for two months continuously, the previously rapid pulse was slowed to fifty beats in the minute; but this was in an elderly man, and accompanied by a sense of increased strength and well-being, with relief of dyspnœa, etc. These were the only two cases in which I could at all obtain any evidence, although I was constantly on the lookout for it, of toxic effects.

As to the other evidences of intoxication mentioned above, nausea occurred in a few cases, but soon passed off; palpitation and præcordial pain certainly result from too large a dose, due probably to the beat laboring against an excessive peripheral resistance, but these symptoms are not produced by smaller doses.

Cough was generally relieved, owing probably to increased depth and regularity of respiratory movements; dyspeptic pains also often diappeared. This I attributed to the improvement of the circulation.

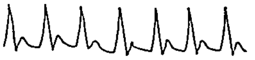
It remains to be said that in cases where the left ventricle is much hypertrophied, or when, from any cause, the heart is beating too violently, spartein quiets and diminishes the force of its action; also that in some instances of abnormally slow pulse, spartein quickens the rate until it reaches or approaches the normal, and finally, that when the arterial tension is already very high, its action is spent in strengthening the heart-beats.

The foregoing seems to lead to the conclusion that spartein belongs to the digitalis group, and acts directly on the cardiac muscle and the cardio-inhibitory centre in the medulla, thus giving rise to increased force of cardiac contractions, and through the pneumogastrics to regulation of the pulse, generally in the direction of slowing; in cases, however, in which the pulse is abnormally slow, the drug often accelerates it. A general rise of arterial tension takes place, partly as the effect of the increased force of the heart-beats, but probably chiefly due to a stimulation of the medullary vasomotor centre causing contraction of the vessels of the splanchnic area, with therefore an increased blood supply to the skin and kidneys. This seems to me the only way in which to explain a general rise of blood-pressure, with, at the same time, a vastly increased quantity of blood driven through the cutaneous vessels. The correlation of skin and kidneys in normal function lends itself to the supposition that at the same time more blood is passing through the renal vessels, thus causing increased excretion of urine. The more marked diuresis produced by larger doses may be due to stimulation of the renal cells, as in the case of digitalis, according to many observers. The quantity of urine is not, however, invariably increased, perhaps in relation with the free diaphoresis produced by spartein in some patients. No effect on the temperature was noted. Tracings from three cases are here given.

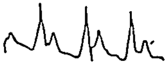
The following tracings[1] were taken at short intervals of time after spartein had been administered.

Case I.—A bad case of mitral regurgitation in a youth of nineteen. The chest was bulged out over the præcordial area, and the area of cardiac dulness was bounded above by the third rib, on the right by the right border of the sternum, and extended beyond the nipple. The apex beat was one inch outside the nipple in the fifth space.

Tracing 1.



Tracing 2.



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[1] Pressure three and a quarter ounces in all tracings.

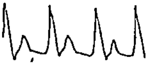
Tracing No. 1. Pulse 120, almost hyperdicrotic; respiration 24; face and lips very livid. Spartein sulph. one-quarter grain administered at 12.45 P.M.

At 1 P.M. there was no change in character of pulse tracings. Pulse 120; respiration 24.

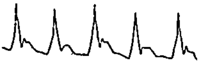
Tracing No. 2. 1.30 P.M. Pulse 90; respiration 24; much less lividity of lips; slight rise of tension.

Tracing No. 3. 2 P.M. Pulse 84; respiration 22; blueness of lips had disappeared; the skin everywhere was now warm and moist, instead of cold as before. A tracing at 2.30 P.M. showed a further rise in tension.

TRACING 3.



TRACING 4.



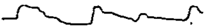
Tracing No. 4. 3.15 P.M. Pulse 84; respiration 20; no lividity; surface of body still warm.

The improvement in appearance was now striking from flushing of the surface. He improved somewhat for three or four weeks, but then made no further advance; the rapidity and violence of the cardiac beats, shortness of breath, etc., increased. The dose of spartein was raised gradually from one-twelfth to one-fourth of a grain, every four hours, without effect. He died after being in bed for one month. Digitalis and other remedies were tried without any benefit.

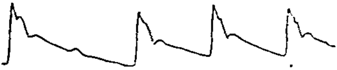
The following tracings are from a case of mitral stenosis.

Tracing No. 5 was taken before administration of spartein. Pulse 72; respiration 18.

TRACING 5.



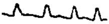
TRACING 6.



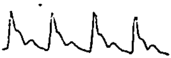
Tracing No. 6 was taken after spartein, one-sixteenth of a grain, had been given every four hours for four days.

The next two tracings are from a case of Graves's disease.

TRACING 7.



TRACING 8.



Tracing No. 7 was taken before the administration of spartein. Pulse-rate was 132; respiration 36.

Tracing No. 8 was taken after sulphate of spartein, one-half grain, had been taken three times a day for five weeks. Pulse 76; respiration 18.

Of ten cases of mitral regurgitation, due in seven to rheumatic fever, in one to endocarditis following chorea, in the other two patients to anæmias associated with violent palpitation, eight were completely relieved, and in the two anæmic patients the murmur disappeared, so that it was probably due to relative incompetence from dilatation of the left ventricle. The two cases that did not improve were very bad ones, and were afterward treated by digitalis, and other measures, without any benefit. The quantity of urine and of urea excreted was increased in six patients. Dyspnœa and præcordial pain appeared to be relieved first, followed by the disappearance of œdema in the most speedy instance after three days' treatment. An increased feeling of well-being was noticed by all, at first even by the two patients in whom the cardiac symptoms were not ameliorated. The pulse was rendered less frequent, stronger, and more regular.

In two or three instances it was found that a small dose, one-sixteenth of a grain, given at intervals of three or four hours, produced the greatest regulating effect on the pulse, and relieved arhythmia where larger and less frequent doses had previously failed to do so. A study of these cases and of others shows that spartein is likely to be of great service in mitral regurgitation, relieving the symptoms in most instances rapidly and completely.

In mitral stenosis we may expect good results when the pulse is small, weak, and irregular, but in this form of heart disease the effect produced by it seems of shorter duration, and more immediately dependent on the continual administration of the drug. Though the patients improved whilst taking it, the good effects ceased on leaving it off. Four out of five cases of mitral stenosis to whom I gave it improved, however; one being able to lie down at night, which had been impossible for three years before.

In one woman, after taking one grain every six hours for three weeks, sharp cutting pains at the left shoulder-blade and over the heart came on, with a feeling of tightness in the chest. These symptoms ceased on reducing the dose.

In aortic regurgitation, when the violent pulsation of a greatly enlarged heart produces much pain and distress, spartein is a valuable remedy, quieting and regulating the excited cardiac action without unduly prolonging the systole; in these cases tracings showed that the excessive force and rapidity of the heart-beats were lessened, *pari passu*, with a gradual fall in the arterial tension. Small doses were here most beneficial. In other forms of hypertrophy it will be found useful when the heart acts violently and irregularly. In the hypertrophy combined with extremely high tension of chronic Bright's disease the effect was to stimulate the cardiac contractions, while the arterial tension was not further raised nor the quantity of urine increased.

In a number of patients suffering from various forms of chronic lung disease with obstruction to the pulmonary circulation, and where compensatory changes had not been established in the right heart, or after being established had broken down, I found spartein of great value; dyspnœa, præcordial pain, and palpitation were relieved almost at once, and in several a cough grew less. In two cases, where there was reason to suspect fatty or other changes of malnutrition in the heart-muscle, no benefit was noted.

Of five cases of asthma, four were entirely relieved, the other was not benefited. The administration of spartein was combined with inhalations of pyridin; improvement was slow, all being under treatment from one to five months. The severity of the symptoms was very much diminished, the attacks cut short, and rendered less frequent after a short time, one to two weeks, and the patients could keep comfortable whilst they continued the drug, but if they left it off were liable to relapse. Gradually the attacks returned less and less often and became milder, and finally ceased at the end of the winter; so that the ultimate effect in four out of five cases was satisfactory, though the slow progress was disappointing after the enthusiastic statements that have been made as to the value of spartein in asthma. In one old man suffering from asthma and chronic bronchitis the pulse-rate, that had previously been 96–84, was slowed to 50 in the minute, and was rendered more forcible. This slowing took place after two months' continuous administration of the drug, and though accompanied by marked amelioration of general symptoms, must be, perhaps, regarded as due to accumulation.

In cases of palpitation, without evidence of organic heart disease, spartein gives immediate relief, which becomes permanent after the remedy has been continued for a week or two. In chlorosis, with dilatation of the heart and the usual murmurs, I found that spartein, given in combination with iron, quickly relieved palpitation, pain, dyspnœa, and œdema of the ankles, and in due course the murmurs and the evidences of dilatation when present disappeared.

The effects of spartein in three cases of Graves's disease were remarkable, and if a wider experience confirms them, it will be a valuable remedy in this disease. In two of the cases the usual remedies, including a long course of arsenic, and the passing of a constant current through the neck, etc., had been tried without effect. On giving spartein the pulse-rate dropped in one week from constant rates of 132 and 136 to the minute, to rates of 72 and 84 respectively, the coincident throbbing and pulsation of the thyroid and of the great vessels of the neck ceased. Other symptoms were relieved, especially the nervousness and weakness previously complained of, and the size of the thyroid tumor distinctly diminished. The gain in strength and general well-being, with improvement of appearance due to gain of flesh and color, was striking.

In the third case, a more severe example of the disease than either of the preceding, there was general improvement, with diminution of violent pulsation in the thyroid and over the neck and face, but the pulse-rate of 144 was not reduced to less than 96 to the minute, varying between this and 108. This patient suffered from continual fine tremor of the muscles, especially in the limbs; while taking spartein this tremor remained absent, but returned if the drug was left off. She has improved in strength and feels well whilst she is taking it. She has now been taking one-quarter of a grain ever four hours for six months.

I gave spartein for periods varying from two weeks to six months in daily quantities of one-third of a grain to twelve grains, the latter large dose was continued in one case for a month with benefit. It is best to begin with one-sixteenth of a grain every four hours, and gradually increase up to two grains, if necessary until the desired effect on the circulation is obtained. When the dose is given less frequently the result does not seem so good; sometimes a large dose may be gradually reduced without loss of effect. There is no fear of accumulation. The signs of an overdose are palpitation, præcordial pain, small, rapid pulse of high tension, and a feeling of great weakness, or even trembling.

Spartein begins to act in about thirty minutes after it has been taken by the mouth, and its action lasts from about five to six hours. This rapidity of action, at first consisting in a stimulation of the heart, rise of arterial tension not occurring until a little later, indicates the use of spartein in asystolic conditions of valvular disease, where a speedy effect is desired, giving it superiority over more slowly acting drugs.

In these conditions, too, a small dose should be employed (one-sixteenth to one-quarter of a grain), since in these doses spartein seems powerfully to stimulate and regulate the heart with the smallest rise of arterial tension, perhaps not more than is the normal accompaniment of increased cardiac force.

Diuretic effect is most marked with fairly large doses, half a grain to two grains; with small it is not so evident, but is often present. Flushing of the surface of the body occurred in from one to two hours after administration in most cases.

THE CARDIAC RELATIONS OF CHOREA.

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The heart symptoms of chorea demand special consideration as among the most important and peculiar features of the disease. Chorea is rarely a fatal disease in children, and hundreds of cases may be treated without